

# PATENT SPECIFICATION

(11) 1303844

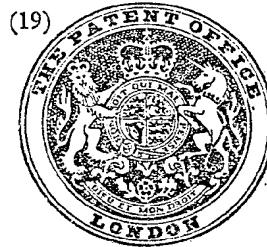
1303844

## NO DRAWINGS

(21) Application No. 6083/70 (22) Filed 9 Feb. 1970  
(31) Convention Application No. 799 109 (32) Filed 13 Feb. 1969 in  
(33) United States of America (US)

(44) Complete Specification published 24 Jan. 1973  
(51) International Classification C07D 5/16, 99/02, 99/04, 99/10  
(52) Index at acceptance

C2C 170—197—285 173—197—288 174—196—288  
175—193—286 17X—186—272 200 213 215  
220 221 222 225 226 22Y 247 250 251  
253 255 256 25Y 28X 305 30Y 311 313 31Y  
332 338 339 342 34Y 351 354 355 35X 360  
361 364 36Y 384 386 401 40Y 579 584 594  
599 59X 602 604 623 624 625 62X 63X 652  
661 662 663 675 697 726 791 79Y KF KP  
KQ KT KY SU UJ



## ERRATUM

### SPECIFICATION NO 1303844

Page 1, lines 24/25 and Page 14, line 23 for R<sub>1</sub> and Y read R and Y

THE PATENT OFFICE  
7 May 1973

R 68612/15

## PATENTS ACT 1949

### SPECIFICATION NO 1303844

The following amendments were allowed under Section 29 on 14 March 1974:-

Page 2, line 29, page 15, line 1, after ketone *insert* or aldehyde

Page 2, line 42, page 3, lines 2 and 8, page 15, lines 9, 10, 13 and 14, after hydroxyketone *insert* or aldehyde

THE PATENT OFFICE  
23 April 1974

R 74662/23

## ERRATUM

### SPECIFICATION NO 1303844

Page 15, line 4, for CH<sub>2</sub>CONR read CH<sub>2</sub>CONR'  
COX COX

THE PATENT OFFICE  
23 April 1974

R 74662/43

SPECIFICATION AMENDED - SEE ATTACHED CLIP

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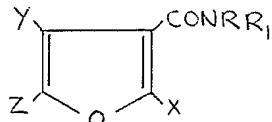


(54) FURAN-3-CARBOXAMIDE DERIVATIVES AND METHOD  
 OF PREPARING SAME

(71) We, UNIROYAL LTD., a corporation of Canada, whose full post office address is P.O. Box 130, Place d'Armes, Montreal, in the Province of Quebec, Canada, do hereby declare the invention, for which we pray that a Patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to a broad class of novel furan-3-carboxamide derivatives which possess good fungicidal and insecticidal properties, and to a novel method for their preparation.

The furan-3-carboxamide derivatives of the invention can be represented by the following formula:



wherein X, Y and Z are the same or different and are selected from H, amino, alkyl, substituted alkyl, alkenyl, phenyl or substituted phenyl or Y and Z together are  $\alpha,\omega$ -alkylene; R is selected from hydrogen, alkyl, acyl, halohydrocarbyl sulphenyl and hydrocarbyl selenyl; R1 is selected from phenyl, substituted phenyl, benzyl, biphenyl, alkyl, alkenyl, cycloalkyl, naphthyl, pyridyl, thiazolyl, ethylene bis- or furfuryl or R and R1 together with the nitrogen atom to which they are attached form a morpholino group, provided that:—

a) R1 is not a phenyl or a tolyl group when, simultaneously, R and Y are hydrogen atoms, X is a methyl group, and Z is a hydrogen atom or a methyl group; b) R1 is not a phenyl group when, simultaneously, R and Z are hydrogen atoms and X and Y are methyl groups; c) R1 is not a phenyl group containing a nitro group as sole substituent or in combination with one or more alkyl or alkoxy substituents when, simultaneously, R, X, Y and Z are hydrogen atoms; and d) R1 is not methyl when, simultaneously, R1 and Y are methyl groups and X and Z are hydrogen atoms.

There are surprisingly few known furan-3-carboxamide derivatives. These include:—

- a) 2-methyl furan-3-N, aminocarboxamide  
 $(X=CH_3, Y \text{ and } Z=H, R=H, R_1=NH_2)$
- b) 2-methyl-furan-3-carboxanilide  
 $(X=CH_3, Y \text{ and } Z=H, R=H, R_1=phenyl)$
- c) 2,4-dimethyl furan 3-carboxanilide  
 $(X \text{ and } Y=CH_3, Z=H, R=H, R_1=phenyl)$

SEE ERRATA SLIP ATTACHED  
 and slip number 2

[Price 25p]

d) 2,4,5-trimethyl furan-3-carboxamide  
(X, Y and Z=CH<sub>3</sub>; R=R<sub>1</sub>=H)  
e) N,N,4-trimethylfuran-3-carboxamide

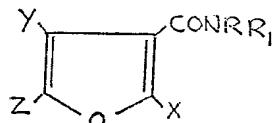
5 None of these known compounds, however, has ever been described as a fungicidal or insecticidal chemical. Their usefulness as such is disclosed and claimed in detail in our British Patent Specification No. 6084/70 (Serial No. 1302410).

10 One useful set of compounds are those in which X, Y and Z are selected from hydrogen alkyl groups containing from 1 to 17 carbon atoms, phenyl, hydroxyalkyl, allyl, alkyl phenyl, alkoxy phenyl, nitrophenyl, and halophenyl, or Y and Z together are tetramethylene; R is selected from hydrogen, methyl, benzoyl and trichloromethyl sulfenyl; R<sub>1</sub> is selected from phenyl, methylphenyl, methoxyphenyl, chlorophenyl, 15 benzyl, biphenyl, alkyl groups containing from 1 to 10 carbon atoms, allyl, cyclohexyl, naphthyl, 2-thiazolyl, 2-pyridyl, ethylene bis- and furfuryl.

15 Preferably, X, Y and Z are methyl, R is H, and R<sub>1</sub> is phenyl; or X, Y and Z are methyl, R is H and R<sub>1</sub> is 2-methylphenyl.

20 Another useful set of compounds of this invention are those in which R is a hydrogen atom and R<sub>1</sub> is a cyclohexyl group.

25 It is a significant and important aspect of the invention that furan-3-carboxamide derivatives, whether new or those few previously known, can be prepared in accordance with a novel one-step method that promises to be of important commercial significance. The present invention thus provides a method of making a compound of the formula:

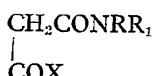


wherein X, Y and Z are the same or different and are selected from hydrogen, amino, 25 alkyl, halo, substituted alkyl, alkenyl, phenyl and substituted phenyl, or Y and Z together are  $\alpha,\omega$ -alkylene; R is selected from hydrogen, alkyl, acyl, and hydrocarbyl sulfenyl; R<sub>1</sub> is selected from phenyl, substituted phenyl, benzyl, biphenyl, alkyl, alkenyl, cycloalkyl, naphthyl, pyridyl, thiazolyl, ethylene bis-, and furfuryl, or R and R' together with the nitrogen atom to which they are attached form a morpholino group, the said method characterized by reacting an  $\alpha$ -hydroxy ketone of the formula



wherein Y and Z are as previously defined

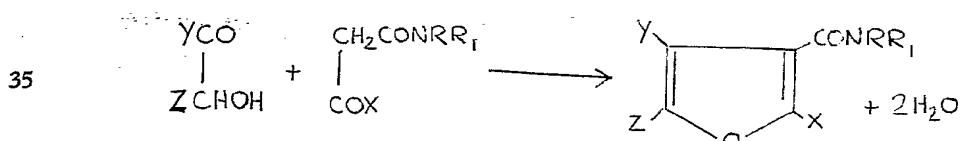
30 with an acetamide of the formula



wherein X, R, R<sub>1</sub> are as previously defined

35 in an inert solvent in the presence of an active Friedel-Crafts reagent.

The preparative reaction sequence is illustrated below:—



40 For example acetoin can be reacted in this way with acetoacetanilide, methyl acetoacetanilide or methoxy acetoacetanilide to form 2,4,5-trimethyl-3-carboxy-anilido furan, 2,4,5-trimethyl-3-(methylcarboxanilido)furan and 2,4,5-trimethyl-3-(methoxycarboxanilido)furan respectively.

45  $AlCl_3$ ,  $AlBr_3$  and  $SnCl_4$  are preferred Friedel-Crafts reagents ( $ZnCl_2$  and  $BF_3$ , for example, tend to produce pyrrole structures). It has been found convenient to use about 0.5 mole of the selected Friedel-Crafts reagent for each mole of  $\alpha$ -hydroxyketone or acetamide used, and to use equimolar quantities of the latter reagents.

45 As the ring closure is accompanied by the expulsion of water, a strongly dehydrating Friedel-Crafts reagent is preferred. On the other hand, it is possible to use just a

catalytic amount of the Friedel-Craft reagent (i.e. 0.01 to 0.50 mole per mole  $\alpha$ -hydroxyketone or acetamide) and to remove the water of reaction by some other means as, for example, by removing it azeotropically in a Dean-Stark trap, or by including an inert dehydrating agent.

5 Since Friedel-Crafts reagents will react with hydroxy groups, it is preferable to employ anhydrous reactants and nonhydroxylic solvents such as, for example, in addition to those mentioned above, nitrobenzene, chlorobenzene, ethyl acetate and acetonitrile.

10 As noted, it is convenient to use equimolar amounts of the  $\alpha$ -hydroxyketone and acetamide reactants. The reaction is exothermic, although some heating at the start of the reaction is preferred; heating to temperatures of about 50°C. or higher suffices. Preferably neither the initial temperature nor the temperature resulting from the heat of reaction should exceed the boiling point of the reacting solution.

15 After completion of the reaction, the reacting solution is quenched with water and hydrochloric acid, the solvent layer is separated, and the product crystallized from solution.

20 The furan-3-carboxamide derivatives can also be made by using the foregoing process to obtain the basic furan-3-carboxamide structure (III), and then employing any well-known substitution reaction to provide a desired radical at any or all of the X, Y and Z positions as well as at the R position.

25 Of course, it must be fully understood that the one step reaction is equally applicable to those few known furan-3-carboxamide derivatives earlier noted, as well as to those novel compounds considered within the scope of the present invention.

20 The following examples illustrate the method of this invention and, with the exception of examples 3 and 8, some of the compounds of this invention.

25 Example 1

2-Methyl-4,5-diphenyl-3-carboxanilidofuran

30 A mixture of 0.05 mole (10.6 g.) benzoin, 0.05 mole (8.9 g.) acetoacetanilide and 0.025 mole (3.3 g.) aluminium chloride was refluxed in 50 ml. benzene with stirring for 30 minutes. The reaction was quenched with water (25 ml.) followed by 25 ml. 6N HCl. The benzene layer was separated, washed with water, then sodium hydroxide and finally water. The product was crystallized from methanol, m.p. 156—159°, yield 28%.

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Example 2

2-Methyl-4,5-dipropyl-3-carboxanilidofuran

35 A mixture of 0.1 mole (14.4 g.) butyroin, 0.1 mole (17.7 g.) acetoacetanilide, 0.05 mole (6.7 g.) aluminium chloride was refluxed and stirred in 50 ml. benzene for 30 minutes. The reaction mixture was treated as in Example 1. The product was crystallized from petroleum ether (60—110°) m.p. 80—82°, yield 28%.

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Example 3

2-Methyl-3-carboxanilidofuran

40 A mixture of 0.05 mole (3 g.) glycolaldehyde, 0.05 mole (8.9 g.) acetoacetanilide, 0.025 mole (3.5 g.) aluminium chloride was heated under reflux and stirred in 35 ml. benzene for 15 minutes. The reaction mixture which turned red was treated as in Example 1. A 45% yield of crude product m.p. 103—108° was obtained.

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Example 4

2,4,5-Trimethyl 3-(o-phenylcarboxanilido) furan

45 A mixture of .05 mole (12.5 g.) o-phenylacetacetanilide, 0.05 mole (4.4 g.) acetoin and .025 mole (3.3 g.)  $\text{AlCl}_3$  in 25 ml. benzene was stirred on a steam bath. Reaction did not appear to take place without warming. After 30 minutes of heating, water was added, followed by dilute hydrochloric acid. The benzene layer was separated, washed with more acid and water, followed by sodium hydroxide and water.

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50 A 72% yield of desired product m.p. 106—108° was obtained by precipitation with petroleum ether.

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Example 5

Preparation of 2,4,5-trimethyl-3-(o-methylcarboxanilido) furan

55 A mixture of 0.1 mole o-methylacetacetanilide (19.1 g.) and 0.1 mole acetoin (8.8 g.) was stirred in 75 ml. toluene on the steam bath. Aluminum chloride (0.05 mole, 6.7 g.) was added in portions. After the initial reaction had subsided, stirring and heating was continued 30 minutes. Dilute hydrochloric acid was added and the two phase system allowed to crystallize. A yield of 76% 2,4,5-trimethyl-3-(o-methylcarboxanilido) furan was obtained m.p. 118.5° after filtration washing and drying.

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## Example 6

## 2,4,5-Trimethyl-3-(o-methoxycarboxanilido) furan

5 A mixture of 0.1 mole o-methoxyacetanilide (20.7 g.) and 0.1 mole acetoin (8.8 g.) was stirred and warmed in 75 ml. toluene while 0.05 mole aluminum chloride (6.7 g.) was added in portions. After stirring and warming on steam bath thirty minutes, dilute hydrochloric acid was added and the product allowed to crystallize. A 70% yield of 2,4,5-trimethyl-3-(o-methoxycarboxanilido) furan m.p. 100.5—102° was obtained after filtering, washing and drying.

## Example 7

## 2,4,5-Trimethyl-3-carboxanilidofuran

10 To a stirred reaction mixture of acetoacetanilide (2 moles, 354 g.), dry acetoin (2 moles, 176 g.) (commercial grade dried by adding benzene, removing the water azeotropically and then removing the benzene by distillation), and dry toluene (1500 ml.) was added aluminum chloride (1 mole 133 g.). The reaction mixture was stirred and 15 cautiously heated to about 50° at which point the heating was discontinued and the temperature quickly rose exothermically to the boiling point. Some hydrogen chloride was evolved through the condenser thus lowering the boiling point of the toluene reaction mixture to about 95°. The reaction mixture was stirred and heated under reflux for one-half hour, allowed to cool to about 85°, water (300 ml.) was cautiously added 20 followed by 6 N hydrochloric acid (ca 200 ml.). The hot reaction mixture was stirred for a few minutes, poured out into a beaker and allowed to cool to room temperature. The precipitate was filtered, washed with dilute hydrochloric acid, with water and with toluene (ca 100 ml) and air dried. The yield of almost white product was 405 g., 25 88%, m.p. 138—139°, concentration of the toluene mother liquors gave a second crop 18 g., 4%, m.p. 134—135°.

## Example 8

## 2,4-Dimethyl-3-carboxanilidofuran

30 A mixture of 0.1 mole (20.1 g.) 2-methyl-3-carboxanilido furan and 0.1 mole (CH<sub>3</sub>COCH<sub>2</sub>OH) (7.4 g.) was stirred at room temperature in 50 ml. benzene. Aluminum chloride (0.1 mole, 13.3 g.) was added. A vigorous reaction of short duration took place and after 15 min. stirring, water was added. The benzene layer was washed with hydrochloric acid, sodium hydroxide and finally water. A 37% yield of 2,4-dimethyl-3-carboxanilidofuran, m.p. 129—130° was obtained.

## Example 9

## 2-Methyl-3-(o-methylcarboxanilido)furan

35 This was prepared as in example 3 from glycolaldehyde (CHOCH<sub>2</sub>OH) and o-methylacetanilide, m.p. 119—121°, yield 55%.

## Example 10

## 2-Methyl-3-(o-methoxycarboxanilido)furan

40 This was prepared from glycolaldehyde and o-methoxyacetanilide in 65% yield as in Example 3; m.p. 61—62°.

## Example 11

## 2-Methyl-5-t-butyl-3-carboxanilidofuran

45 A mixture of 0.1 mole (10.1 g.) 2-methyl-3-carboxanilido furan and 0.1 mole (13.7 g.) t-butylbromide was stirred in 200 ml. carbon disulfide in an ice bath. 0.15 Mole (19.1 g.) aluminum chloride was added portion wise. The mixture was then stirred at room temperature for 8 hours and let stand over night. It was poured onto ice and the precipitate filtered off and crystallized from xylene to give a 68% yield of 2-methyl-5-t-butyl-3-carboxanilidofuran, m.p. 151—152.5°.

## Example 12

## 2-Methyl-3-carboxanilido-4,5,6,7-tetrahydrobenzofuran:

50 A mixture of 0.1 mole (21.5 g.) 2,4-dimethyl-3-carboxanilidofuran and 0.1 mole (13.7 g.) t-butyl bromide was stirred in 200 ml. carbon disulfide at room temperature and 0.15 mole (19.1 g.) aluminum chloride added portion-wise. The mixture was stirred 6 hours, let stand over night and then poured into ice. The carbon disulfide layer was separated, the aqueous layer was extracted with ether and added to it. Petroleum ether (60—110°) was added to give 22 g. of white precipitate m.p. 127—142°. The product was washed with a few ml. hot petroleum ether, to give a 30% yield of 2,4-dimethyl-5-t-butyl-3-carboxanilidofuran, m.p. 143—147°.

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## Example 13

## 2-Methyl-3-carboxanilido-4,5,6,7-tetrahydrobenzofuran:

5 A mixture of 0.1 mole (11.4 g) 2-hydroxycyclohexanone, 0.1 mole (17.7 g) of acetoacetanilide, 0.05 mole (6.7 g) aluminum chloride and 75 ml. of benzene was heated under reflux for 30 minutes. The reaction mixture was worked up as in example 1. The product was crystallized from benzene-petroleum ether (60—110°), m.p. 119—120°, yield 75%.

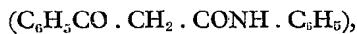
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## Example 14

## 2-Phenyl-4,5-methyl-3-carboxanilidofuran:

10 This was prepared as above from benzoylacetanilide

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acetoin and aluminum chloride using toluene as solvent. The product melted at 167—169° after crystallization from methanol, yield 34%.

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## Example 15

## 2,4,5-Trimethyl-3-p-fluorocarboxanilidofuran:

This was prepared as above from p-fluoroacetoacetanilide, acetoin and aluminum chloride using benzene as solvent. The product melted at 170.5—171.5, after crystallization from toluene, yield 80%.

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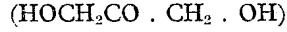
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## Example 16

## 2-Methyl-4-hydroxymethyl-3-carboxanilidofuran:

This was prepared as above from acetoacetanilide, dihydroxyacetone

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and aluminum chloride using benzene as solvent. The product melted at 120—122° after crystallization from benzene petroleum ether (60—110), yield 7%.

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## Example 17

## 2,4,5-Trimethyl-3-carboxanilido-N-benzoylfuran:

To a solution of 2,4,5-trimethyl-3-carboxanilidofuran (15 g) in chloroform (150 ml) was added benzoyl chloride (15 g) and triethylamine (15 ml) and the solution was heated under reflux for 20 hours. The reaction mixture was cooled, washed with aqueous sodium hydroxide and with water and the solvent was removed. The residue which solidified was crystallized twice from isopropanol yielding 8 g of white prisms melting at 120—121°.

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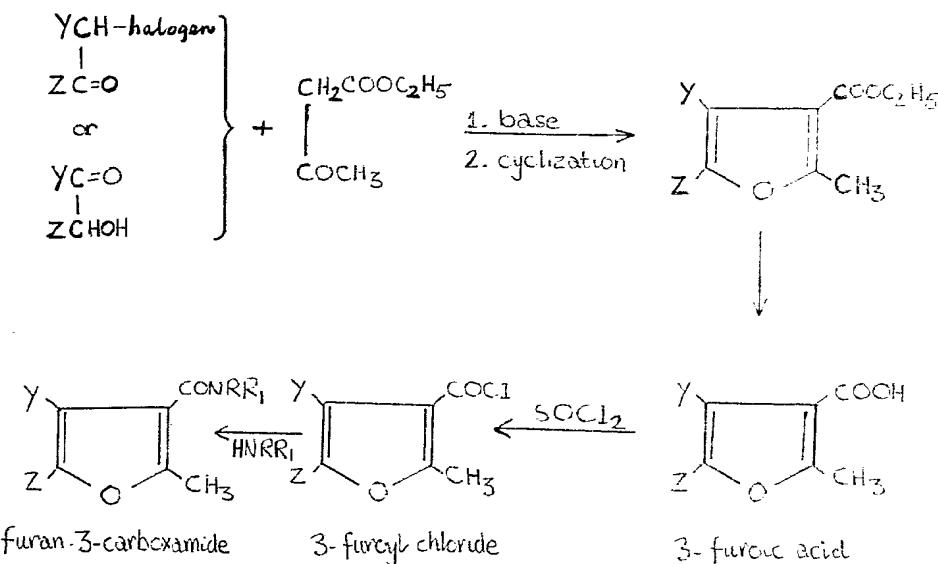
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Yet another process can be used in making the compounds of the invention. However, this alternate process involves many steps and hence is decidedly inferior to the one step process described above. The multi-step process involves: (1) the reaction of an  $\alpha$ -chloroketone or an  $\alpha$ -hydroxyketone with ethyl acetoacetate to produce the furan-3-carboxylate; (2) the conversion of the product to the corresponding 3-furoic acid (3) the conversion of the acid into the corresponding 3-furoyl chloride by thionyl chloride, phosphorous pentachloride or other halogenating agents in inert solvents; (4) followed by conversion of the 3-furoyl chloride to a furan-3-carboxamide by treatment with a primary or secondary amine in an inert solvent.

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The steps required to obtain the 3-furoic acid are well known. (See H. E. Winberg et al, J. Am. Chem. Soc. 82, 1428 (1960); F. G. González et al, Anal. real. Soc. españ. Fis Quím. 50B 407 (1954); C.A. 49 13206h (1955); O. Dann et al, Ber. 85 457 (1952); J. C. Hanson et al, J. Chem. Soc. 1965 5984; and R. M. Acheson et al, J. Chem. Soc. 1952 1127-33.)

The following examples demonstrate the multi-step method.

Example 18

2-Methyl-3-N-allylcarboxamidofuran

10 Diethyl chloroacetal (1 mole, 152.6 g.), and water (200 ml.), containing 6N hydrochloric acid (20 ml.) were heated under reflux (about 2 hours) until solution resulted. The acidic solution containing chloroacetaldehyde was neutralized with pyridine and added to a solution of ethyl acetoacetate (1 mole, 130 g.) in pyridine (250 ml.) and stirred at room temperature for four hours. The oily layer containing ethyl 2-methyl-3-furoate was separated, washed with dilute hydrochloric acid and saponified by heating with a solution of sodium hydroxide (50 g.) in water (300 ml.) and ethanol (300 ml.) for 4 hours. Acidification of the ethanolic solution precipitated 2-methyl-3-furoic acid which was filtered, washed and dried, m.p. 103-106°.

15 2-Methyl-3-furoic acid (0.1 mole, 12.6 g.) was suspended in benzene (50 ml.), thionyl chloride (0.11 mole, 13 g.) was added and the reaction mixture was allowed to stand at room temperature for about twenty hours. The excess thionyl chloride and solvent were removed under reduced pressure. To the residue was added portion wise with cooling a solution of allylamine (0.2 mole, 11.4 g.) in about 50 ml. benzene and the reaction mixture let stand at room temperature for three hours. The benzene solution was washed with dilute hydrochloric acid and then diluted with petroleum ether (60-110°) to precipitate 2-methyl-3-N-allylcarboxamidofuran, m.p. 46-47°; yield 14 g. or 80%.

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Example 19

2,5-Dimethyl-3-carboxanilidofuran

30 To a stirred and refluxing solution of ethyl sodioacetoacetate (0.5 mole, 76 g.) and sodium iodide (1 g.) in dry acetone (250 ml.) was added chloroacetone (0.54 mol. 50 g.) over a period of ten minutes. After one hour the acetone was distilled from the reaction mixture and the residue was diluted with 400 ml. water. The precipitated oil was extracted with ether and the ether removed to yield the intermediate 3-carbethoxy-2,5-hexanedione (75 g.). The intermediate (26.4 g.) was cyclized by heating under reflux over 5 g. anhydrous oxalic acid for 1 1/4 hours. The crude ester was saponified by heating under reflux for 45 minutes with potassium hydroxide (26 g.) in methanol (200 ml.). The methanol was removed, the residue dissolved in water and the solution acidified to yield 2,5-dimethyl-3-furoic acid (18 g.), m.p. 130-133°.

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40 The acid (0.1 mole, 15 g.) was dissolved in chloroform, the solution treated with

excess thionyl chloride and allowed to stand at room temperature overnight. The excess thionyl chloride and solvent were removed under reduced pressure, the residual acid chloride dissolved in benzene and the solution treated with aniline (0.2 mole, 18.6 g.) in benzene solution decolorized with "Norit" (Registered Trade Mark) and diluted with petroleum ether to precipitate the title compound (17 g.) m.p. 93—94°. 5

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Example 20

2,4,5-Trimethyl-3-N,N-diethylcarboxamidofuran

(1) 2,4,5-Trimethyl-3-furoic acid

10 A mixture of 3-hydroxy-2-butanone (90 g.) ethyl acetoacetate (175 g.), absolute ethanol (150 ml.) and anhydrous zinc chloride (100 g.) was heated under reflux for 24 hours. The cooled solution was poured into water and extracted with benzene. The benzene extract was washed successively with 30% aqueous sodium bisulfite, 5% sodium hydroxide, dilute hydrochloric acid and finally with water. The solvent was removed and the residual ester saponified with aqueous-alcoholic alkali as in example 18 to yield 149 g. or 96% yield of the 2,4,5-trimethyl-3-furoic acid. 15

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(2) 2,4,5-Trimethyl-3-furoic acid

20 To a stirred and refluxing solution of ethyl sodioacetoacetate (153 g.), sodium iodide (2 g.) and dry acetone (500 ml.) was added 3-chloro-2-butanone (1.1 mol., 117 g.) and the refluxing and stirring continued for 1 1/2 hours. The precipitated sodium chloride was filtered off from the reaction mixture and the acetone was removed from the filtrate. To the residue, water was added and the oily intermediate extracted with benzene. The benzene solution was treated with p-toluenesulfonic acid (0.5 g.) and heated under reflux collecting the water of cyclization-dehydration in a Dean-Stark trap. After the reaction was completed (2—4 hours) the benzene was removed and the residual ester was saponified as in example 18 to give 117 g. (yield 76%) of 2,4,5- trimethylfuroic acid. 25

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25 The acid (0.1 mole, 15.4 g.) was suspended in benzene, the solution treated with thionyl chloride (13 g.) and allowed to stand at room temperature overnight. The excess thionyl chloride and solvent were removed under reduced pressure, the residue treated with diethylamine (0.2 mole, 14.8 g.) in benzene (50 ml.) with cooling and the reaction mixture was allowed to stand at room temperature for three hours. The benzene solution was washed with 5% aqueous sodium hydroxide, with dilute hydrochloric acid and with water. The solvent was removed to yield the oily title compound (10 g., 48%). 30

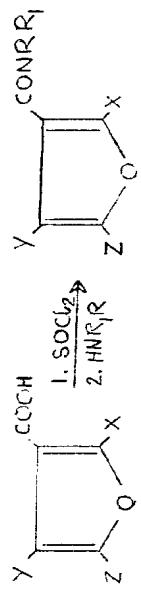
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Example 21

2-n-Heptadecyl-4,5-dimethyl-3-carboxanilidofuran

35 2-n-Heptadecyl-4,5-dimethyl-3-carboxyfuran was prepared from ethyl stearoyl-acetate and 3-hydroxy-2-butanone as in example 20. This was converted to the anilide via the acid chloride in the usual manner. The yield was 30%. 35

## Other examples of Furan-3-Carboxanilides

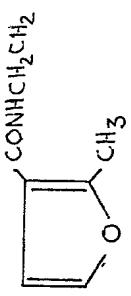


Example No.	Name of the 3-substituent	R	R <sub>1</sub>	X	Y	Z	m.p.
22	N-Isopropyl-carboxamido	H	—CH(CH <sub>3</sub> ) <sub>2</sub>	CH <sub>3</sub>	H	H	84—86
23	N-n-Butyl-carboxamido	H	—C <sub>4</sub> H <sub>9</sub>	CH <sub>3</sub>	H	H	oil
24	N-Cyclohexylcarboxamido	H		CH <sub>3</sub>	H	H	99—100
25	m-Methyl-carboxanilido	H		CH <sub>3</sub>	H	H	91—91.5
26	p-Methyl-carboxanilido	H		CH <sub>3</sub>	H	H	80—82°

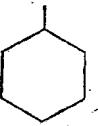
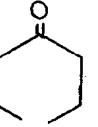
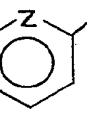
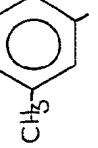
Other examples of Furan-3-Carboxanilides Cont.

Example No.	Name of the 3-substituent	R	R <sub>1</sub>	C	Y	Z	m.p.
27	m-Methoxy-carboxanilido	H		CH <sub>3</sub>	H	H	oil
28	p-Methoxy-carboxanilido	H		CH <sub>3</sub>	H	H	108—109°
29	p-Nitro-carboxanilido	H		CH <sub>3</sub>	H	H	179—180
30	<i>o</i> -Phenylcarboxanilido						oil
31	N-2-Thiazolylcarboxamido	H		CH <sub>3</sub>	H	H	162—163.5

## Other examples of Furan-3-Carboxanilides— Cont.

Example No.	Name of the 3- Substituent	R	R <sub>1</sub>	X	Y	Z	m.p.
32	2,6-Dimethylcarboxanilido	H			CH <sub>3</sub>	H	146—148°
33	2,4,6-trimethylcarboxanilido	H			CH <sub>3</sub>	H	155—156
34	ethylene bis-	H			CH <sub>3</sub>	H	174—175
35	N-Allyl-carboxamido	H	CH <sub>2</sub> =CHCH <sub>2</sub> —		CH <sub>3</sub>	CH <sub>3</sub>	70—72°
36	N-Isopropylcarboxamido	H	—CH(CH <sub>3</sub> ) <sub>2</sub>		CH <sub>2</sub>	CH <sub>3</sub>	718—120°
37	N-n-Butylcarboxamido	H	N-C <sub>4</sub> H <sub>9</sub>		CH <sub>3</sub>	CH <sub>3</sub>	77—79
38	N-n-Decylcarboxamido	H	C <sub>10</sub> H <sub>21</sub>		CH <sub>3</sub>	CH <sub>3</sub>	oil

## Other examples of Furan-3-Carboxanilides Cont.

Example No.	Name of the 3-substituent	R	R <sub>1</sub>	X	Y	Z	m.p.
39	N-Benzylcarboxamido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	104—106
40	N-Cyclohexylcarboxamido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	158—160
41	Carboxmorpholido	R & R <sub>1</sub> together		CH <sub>3</sub>	CH	CH <sub>3</sub>	59—61°
42	N-2-Pyridylcarboxamido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	116—118°
43	N-Methylcarboxanilido	CH <sub>3</sub>		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	oil
44	m-Methylcarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	131—132°

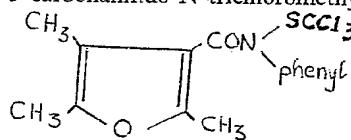
## Other examples of Furan-3-Carboxamides—Cont.

Example No.	Name of the 3-substituent	R	R <sub>1</sub>	X	Y	Z	m.p.
45	n-Methoxycarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	95—97°
46	p-Methoxycarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	162—163.5°
47	p-Chlorocarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	175—177
48	$\alpha$ -Naphthylcarboxamido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	145—146
49	$\beta$ -Naphthylcarboxamido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	142—144

## Other examples of Furan-3-Carboxanilides—Cont.

Example No.	Name of the 3-substituent	R	R <sub>1</sub>	X	Y	Z	m.p.
50	2,6-Dimethylcarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	143.5—145°
51	2-Methyl-6-chlorocarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	147—148.5°
52	2,4,6-Trimethylcarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	144—146°
53	Carboxanilido	H	C <sub>6</sub> H <sub>5</sub>	C <sub>3</sub> H <sub>7</sub>	CH <sub>3</sub>	CH <sub>3</sub>	127—128.5°
54	Carboxanilido	H	3 <sub>6</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub>	CH <sub>3</sub>	CH <sub>3</sub>	168—169°
55	N-Furfurylcarboxanilido	H		CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>	96—97°

Example 56  
2,4,5-trimethyl-3-carboxanilido-N-trichloromethylsulfonylfuran:



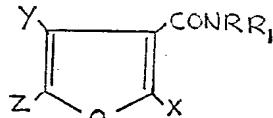
5 2,4,5-trimethyl-3-carboxanilidofuran was heated in a benzene solution with sodium hydride until the evolution of hydrogen ceased; excess trichloromethylsulfonyl chloride ( $\text{Cl}_2\text{CSCl}$ ) was added and heat was again applied to produce the product. m.p. 92—94°C.

5

## WHAT WE CLAIM IS:—

1. A compound characterized by the formula:

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wherein X, Y and Z are the same or different and are selected from H, amino, alkyl, substituted alkyl, alkenyl, phenyl, or substituted phenyl or Y and Z together are  $\alpha,\beta$ -alkylene; R is selected from hydrogen, alkyl, acyl, halo hydrocarbyl sulfenyl and hydrocarbyl sulfenyl; R' is selected from phenyl, substituted phenyl, benzyl, biphenyl, alkyl, alkenyl, cycloalkyl, naphthyl, pyridyl, thiazolyl, ethylene bis- or furfuryl or R and R' together with the nitrogen atom to which they are attached form a morpholino group, provided that:— a) R' is not a phenyl or a tolyl group when, simultaneously, R and Y are hydrogen atoms, X is a methyl group and Z is a hydrogen atom or a methyl group, b) R' is not a phenyl group when, simultaneously, R and Z are hydrogen atoms and X and Y are methyl groups; c) R' is not a phenyl group containing a nitro group as sole substituent or in combination with one or more alkyl or alkoxy substituents when, simultaneously, R, X, Y and Z are hydrogen atoms; and d) R' is not methyl when, simultaneously, R' and Y are methyl groups and X and Z are hydrogen atoms.

15

2. A compound according to Claim 1 characterized in that X, Y and Z are selected from hydrogen, alkyl groups containing from 1 to 17 carbon atoms, phenyl, hydroxyalkyl, allyl, alkyl phenyl, alkoxy phenyl, nitrophenyl and halophenyl, or Y and Z together are tetramethylene; R is selected from hydrogen, methyl, benzoyl and trichloromethyl sulfenyl; R' is selected from phenyl, methylphenyl, methoxyphenyl, chlorophenyl, benzyl, biphenyl, alkyl groups containing from 1 to 10 carbon atoms, allyl, cyclohexyl, naphthyl, 2-thiazolyl, 2-pyridyl, ethylene bis- and furfuryl.

20

3. A compound according to Claim 2 characterized in that X, Y and Z are methyl, R is H, and R' is phenyl.

25

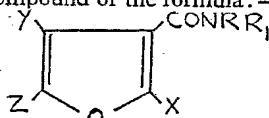
4. A compound according to Claim 2 characterized in that X, Y and Z are methyl, R is H, and R' is 2-methylphenyl.

30

5. A compound according to Claim 1 characterized in that R is a hydrogen atom and R' is a cyclohexyl group.

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6. A method of making a compound of the formula:—



40 wherein X, Y and Z are the same or different and are selected from hydrogen, amino, alkyl, halo, substituted alkyl, alkenyl, phenyl and substituted phenyl, or Y and Z together are  $\alpha,\beta$ -alkylene; R is selected from hydrogen, alkyl, acyl, and hydrocarbyl sulfenyl; R' is selected from phenyl, substituted phenyl, benzyl, biphenyl, alkyl, alkenyl, cycloalkyl, naphthyl, pyridyl, thiazolyl, ethylene bis-, and furfuryl, or R and R' together with the nitrogen atom to which they are attached form a morpholino

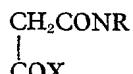
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group, the said method characterized by reacting an  $\alpha$ -hydroxy ketone of the formula



wherein Y and Z are as previously defined

with an acetamide of the formula



wherein X, R, R' are as previously defined

5 in an inert solvent in the presence of an active Friedel-Crafts reagent. 5

7. A method according to Claim 6 characterized in that said Friedel-Crafts reagent is selected from the group consisting of  $\text{AlCl}_3$ ,  $\text{AlBr}_3$  and  $\text{SnCl}_4$ .

8. A method according to Claim 6 or Claim 7 characterized in that about equimolar amounts of said  $\alpha$ -hydroxyketone and acetamide are used, and about 0.5 mole of said Friedel-Crafts reagent is present for each mole of  $\alpha$ -hydroxyketone or acetamide. 10 10

9. A method according to any one of Claims 6 to 8 characterized in that about equimolar amounts of said  $\alpha$ -hydroxyketone and acetamide are used, and from 0.01 to 0.5 mole of said Friedel-Crafts reagent is present for each mole of  $\alpha$ -hydroxyketone or acetamide, together with means for removing water formed by the reaction. 15 15

10. A method according to any one of Claims 6 to 9 characterized in that said  $\alpha$ -hydroxyketone is acetoin and said acetamide is acetoacetanilide, whereby 2,4,5-trimethyl-3-carboxy anilidofuran is produced.

11. A method according to any one of Claims 6 to 9 characterized in that said  $\alpha$ -hydroxyketone is acetoin and said acetamide is methylacetoacetanilide, whereby 2,4,5-trimethyl-3-(methylcarboxanilido)furan is produced. 20 20

12. A method according to any one of Claims 6 to 9 characterized in that said  $\alpha$ -hydroxyketone is acetoin and said acetamide is methoxy-acetoacetanilide, whereby 2,4,5-trimethyl-3-(methoxy-carboxanilido)furan is produced.

13. A compound according to Claim 1 substantially as herein described. 25 25

14. A compound according to Claim 1 substantially as herein described with reference to any one of the foregoing Examples, with the exception of Examples 3 and 8.

15. A method according to Claim 6 substantially as herein described.

16. A method according to Claim 6 substantially as herein described with reference to any one of the foregoing Examples 1—55. 30 30

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